

REMARKS

Reconsideration is requested.

Claim 55 has been amended, without prejudice, to advance prosecution.

Support for the unamended claim 55 may be found throughout the specification as previously noted in the remarks of record. The claims are supported by an adequate written description and withdrawal of the Section 112, first paragraph "written description", rejection of claim 55 and claims dependent therefrom is requested. The Examiner's reference to claims 77-80 on page 3 of the Office Action dated May 21, 2009, is not clear as claims 77-80 had been previously canceled, without prejudice. The Examiner's comments with regard to claims 71-73 and support for same are noted. Consideration of the following comments, in addition to the previously-submitted remarks, are requested with regard to the written description support in the specification for the subject matter of claims 71-73.

The invention relates, for example, to three discrete HCV region relating to Core, NS4 and NS5. Three groups of overlapping peptides which are claimed in this respect are:

- i) Core: peptides I (aa 1-20); II (aa 7-26); III (aa 13-32); IV (aa 37-56); V (aa 49-68); VI (aa 61-80) and VII (aa 73-92)
- ii) NS4: peptides VIII (aa 1688-1707); IX (aa 1694-1713); X (aa 1706-1725); XI (aa 1712-1731); XII (aa 1718-1737); XIII (aa 1724-1743) and XIV (aa 1730-1749)

iii) NS5: peptides XV (aa 2263-2282); XVI (aa 2275-2294); XVII (aa 2287-2306); XVIII (aa 2299-2318) and XIX (aa 2311-**2330**)

The boundaries of each region correspond to the regions described in claims 71-73:

- i) aa 1-92 correspond to the combination of overlapping peptides I to VII, defining the discrete immunogenic region in Core
- ii) aa 1688-1749 correspond to the combination of overlapping peptides VIII to XIV, defining the discrete immunogenic region in NS4
- iii) aa 2263-2330 correspond to the combination of overlapping peptides XV to XIX, defining the discrete immunogenic region in NS5

On page 5, lines 11-17 of the specification, the applicants describe their invention as including amino acids which may be added to the N- or C-terminus of the peptides, which would allow for the gap between peptide III and IV, for example, to be closed.

As such, the claimed regions in claims 71-73 represent the combination of the individual peptides described by the discrete, distinct and clearly identifiable individual regions. The claimed regions in claims 71-73 thus do not represent mere random combinations of several of the claimed peptides. They define the boundaries of the demonstrated immunogenic regions according to the invention.

Page 4, lines 7-8 of the application describes the following:

"It may also be desirable in certain instances to join two or more peptides together in one peptide structure".

In this respect, the combination of peptides VIII, IX, XI, XIII and XIV (corresponding to aa 1688-1749) as well as the combination of peptides XV, XVI, XVII, XVIII and XIX (corresponding to aa 2263-2330) are **explicitly disclosed** as particularly advantageous in the application (see page 11, lines 8-9 of the application).

Withdrawal of the Section 112, first paragraph "written description", rejection of claims 55, 59, 60, 62, 68-73 and 81-89 is requested.

The Section 102 rejection of claims 55, 59, 60, 62, 68-73 and 81-89 over Houghton (U.S. Patent No. 5,350,671), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The Examiner is requested to respond to the applicants previous remarks relating to the applicability of, for example, MPEP § 1701 in the event the Examiner continues to reject the claims over previously-cited art. The Examiner's basis for the rejection appears to be one of disbelief that prior Patent Office Examiners adequately found the patentable aspects of the pending claims to define over the cited art. The applicants should not be required, according to MPEP § 1701, to demonstrate the validity of the previously issued claims.

The invention relates to three sets of overlapping peptides, each set confined with in a specific region of HCV (*i.e.*, Core, NS4 and NS5). In this respect, the subject-matter of claim 55 relates to a combination of distinct molecules comprising:

- (1) a first molecule comprising at least 5 amino acids derived from a distinct part of the Core region,

A second molecule comprising at least 5 amino acids derived from a distinct part of the NS4 region, and

A third molecule comprising at least 5 amino acids derived from a distinct part of the NS5 region;

Further including

(2) at least one molecule consisting of at least 5 amino acids from one of the above claimed peptides

The following table illustrates a comparison between the presently claimed peptides and corresponding peptides as suggested by Houghton. None of the claimed peptides is explicitly disclosed by Houghton. The Section 102 rejection should be withdrawn as the cited document fails to teach each and every aspect of the claimed invention. The additional molecule which is present in the combination, is not anticipated by Houghton.

HCV region	AA-AA of Houghton et al.	Claimed amino acid positions	
		Peptide	AA position
Core	AA1-AA25	I, II	1-20, 7-26
	AA5-AA20	IIa	8-18
	AA1-AA50	III	13-32
	AA1-AA84	IV	37-56
	AA45-AA65	V	49-68
	AA65-AA75	VI	61-80
	AA80-AA92	VII	73-92

NS4	AA1690-AA1720	VIII, IX, X	1688-1707, 1694-1713, 1706-1725
	AA1694-AA1735	XI, XII	1712-1731, 1718-1737
	AA1720-AA1745	XIII, XIV	1724-1743, 1730-1749
NS5	AA2265-AA2280	XV	2263-2282
	AA2250-AA2330	XVI	2275-2294
	AA2290-AA2310	XVII, XVIII	2287-2306, 2299-2318
	AA2310-AA2330	XIX	2311-2330

Houghton lists on column 28, line 67 – column 29, line 68 an extensive list of peptides which **may** be used as an HCV epitope. On column 28, lines 55-58 Houghton states: *"It is to be understood that these peptides do not necessarily precisely map one epitope, but may also contain HCV sequence that is not immunogenic".*

Houghton fails to describes the specific combinations of the claimed invention. The present invention claims 19 peptides, which can be grouped into three discrete HCV regions: Core, NS4 and NS5. The presently claimed invention defines a limited set of peptides, located in a limited group of regions. Houghton does not describe any particular regions, nor does Houghton suggest that peptides from Core, NS4 and NS5 would be particularly useful as epitopes, as combinations of the present claims.

Houghton does not disclose the combinations of peptides, from distinct regions of HCV, as claimed.

The present invention relates to **combinations of specific peptides located within specific HCV regions**. It has been found that combinations of specific peptides from the Core, NS4 and NS5 regions are particularly useful for diagnostic assays.

Page 16, lines 7-14 of the specification describes the following"

"While it is evident that some of the peptides are recognized by a large percentage of sera from HCV-infected individuals, it is also clear that no single peptide is recognized by all sera. In contrast, the peptide mixture was recognized by all fifteen sera, and for six of the 15 sera, the optical densities obtained were equal or higher than those obtained for any of the peptides individually. These results serve to illustrate the advantages of using mixtures of peptides for the detection of anti-HCV antibodies."

In addition to evaluating the mixtures in comparison to the individual peptides, a comparison was made between the claimed mixtures and a commercially available peptide-based ELISA. In this respect, page 18, lines 18-26 of the specification as originally filed states:

"Of the twenty-nine samples tested, twenty-five (86%) were positive in the peptide-based ELISA and recognized one or more nylon-bound peptides. In contrast, only fourteen of the twenty-nine sera scored positive in the commercially available ELISA. These results serve to illustrate the advantages of using peptide mixtures for the detection of anti-HCV antibodies as well as the need to include in the mixtures peptides which contain amino acid sequences derived from different regions of the HCV polyprotein."

Thus, as well as not being disclosed by Houghton, the claimed peptide combinations are superior in performance as compared to existing commercially available assays.

Evidence that the claimed peptides are superior over the peptides disclosed by Houghton has already been presented to the Examiner in the form of additional data presented in the Amendment of November 2, 2007. The Examiner did not find these data convincing (see Office Action of February 5, 2008, page 5) and stated that the claimed peptides allegedly performed similar to the peptides disclosed by Houghton.

The applicants are concerned however that the Examiner did not appreciate the additional data correctly. The additional data clearly demonstrate that more HCV positive sera can be detected with the claimed peptides in comparison with the corresponding peptides as disclosed by Houghton by ELISA and/or LIA. Furthermore, the immune response to HCV is multispecific. In order to detect most of the HCV-infected cases, the use of multiple epitopes is required. Therefore, an additional reactivity of one peptide with 5% of HCV positive cases is considered as a major advantage in the screening and confirmation of HCV antibodies. An overall additional detection of 1% of HCV positive cases, or even 0.1% or only a few cases out of millions of blood donations, is already considered as a very competitive advantage of the assay.

The claims of the present application define **combinations** of peptides. As such, small differences in performance of individual peptides will additively be magnified in combinations of such peptides.

The cited art fails to teach each and every aspect of the claimed invention.

Withdrawal of the Section 102 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

DeLeys et al
Appl. No. 10/822,871
Atty. Ref.: 2551-141
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The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

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